REPUBLIC OF SOUTH AFRICA
REVENUE
13.12.96
R 24.00
INKOMSTE
REPUBLIEK VAN SUID AFRIKA

JOHN & KERNICK
P O Box 3514
HALFWAY HOUSE
1685

FORM P1

REPUBLIC OF SOUTH AFRICA
PATENTS ACT, 1978
APPLICATION FOR A PATENT AND ACKNOWLEDGEMENT OF RECEIPT
(Section 30(1) - Regulation 39)

The grant of a Patent is hereby requested by the undermentioned applicant(s) on the present application filed in duplicate

M 17669

21 01 Official Application No	22 Lodging Date	47 J & K Reference
9610519	13 December 1996	AP 32488 ZA

71 Full name(s) of applicant(s)

BAYER AKTIENGESELLSCHAFT, a legal body organised and existing under the laws of Federal Republic of Germany

Address(es) of applicant(s)

Leverkusen, D-51368, Federal Republic of Germany

54 Title of Invention

PROCESS FOR THE PREPARATION OF SYNTHETIC PYRETHROIDS BY AZEOTROPIC ESTERIFICATION

- [X] The applicant claims priority as set out in the accompaning form P2. The earliest priority claimed is DE 195 46 920.8 15 December 1995
- [ ] This application is for a Patent of Addition to Patent Application No. 24 01
- [ ] This application is a fresh application in terms of S 37 and based on Application No. 21 01

This application is accompanied by:

- [ ] 1a A single copy of a provisional specification of pages
- [X] 1b Two copies of a complete specification of 8 pages
- [ ] 2a Informal drawings of sheets
- [ ] 2b Formal drawings of sheets
- [X] 3. Publication particulars and abstract (form P8 in duplicate)
- [ ] 4. A copy of Figure of the drawings for the abstract
- [X] 5. Assignment of invention (from the Inventors) or other evidence of title
- [X] 6. Certified priority documents (1 documents)
- [X] 7. Translation of priority documents (1 documents)
- [ ] 8. Assignment of priority rights
- [ ] 9. A copy of form P2 and the specification of S.A. Patent Application 21 01
- [X] 10. A declaration and power of attorney on form P3
- [ ] 11. Request for ante-dating on form P4
- [ ] 12. Request for classification on form P9
- [ ] 13a Request for delay of acceptance on form P4
- [ ] 13b

74 Address for Service: JOHN & KERNICK, Midrand.

Date 13 December 1996

For the Applicant

The duplicate will be returned to the applicant for service as proof of lodging but is not valid unless endorsed with official stamp.

Official date stamp
REGISTRAR OF PATENTS, DESIGNS, TRADE MARKS AND COPYRIGHT
13 DEC 1996
Registrar of patents
REGISTRATEUR VAN PATENTE, MODELLE, HANDELSMERKE EN OUTEURSREG

FORM P7

REPUBLIC OF SOUTH AFRICA
PATENTS ACT, 1978

JOHN & KERNICK
P O Box 3511
HALFWAY HOUSE
1685

COMPLETE SPECIFICATION

(Section 30(1) - Regulation 28)

21 01 Official Application No	22 Lodging Date	47 J & K Reference
9610519	13th December 1996	AP 32488 ZA

51 International Classification	
C07C	

71 Full name(s) of applicant(s)

BAYER AKTIENGESELLSCHAFT, a legal body organised and existing under the laws of Federal Republic of Germany

72 Full name(s) of inventor(s)

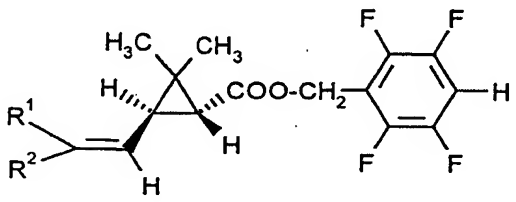
Mattias DECKER, Michael ESSER, Martin LITTMANN, Hans-Peter SEHNEM

54 Title of Invention

PROCESS FOR THE PREPARATION OF SYNTHETIC PYRETHROIDS BY AZEOTROPIC ESTERIFICATION

Process for the preparation of synthetic pyrethroids by azeotropic esterification

The present invention relates to a novel process for the preparation of synthetic pyrethroids of the formula (I)



(I)

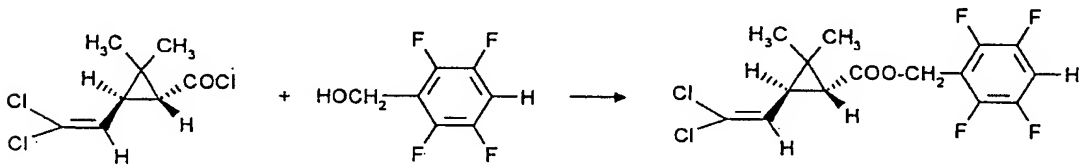
in which

R^1 represents methyl, difluoromethyl, trifluoromethyl or chlorine and

R^2 represents methyl, difluoromethyl, trifuoromethyl or chlorine, by azeotropic esterification.

Compounds of this type have achieved importance, in particular in controlling insects.

DE 37 05 224 discloses the reaction of the acid chloride of (+)-trans-permethric acid with 2,3,5,6-tetrafluorobenzyl alcohol according to the following reaction scheme:

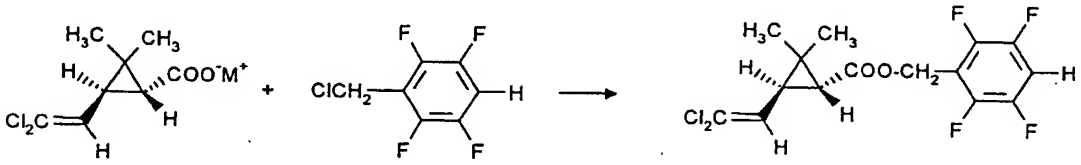


In the process, the D-menthyl ester of (+)-trans-permethric acid is saponified in methanol/sodium hydroxide solution. After the methanol is distilled off, water is added and the D-menthol is extracted with toluene. After acidification of the aqueous phase, the (+)-trans-permethric acid is extracted with toluene.

The toluene solution is distilled until it is free of water and then thionylochloride is added. Toluene and excess thionyl chloride are then distilled off; (+)-trans-permethryl chloride remains in the bottom phase.

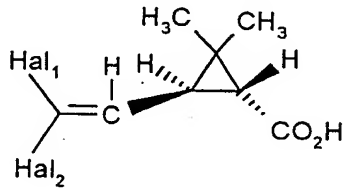
The acid chloride is pumped to the tetrafluorobenzyl alcohol introduced, reacting to form transfluthrin. The product is firstly subjected to a steam distillation, then diluted with toluene and the toluene solution is stirred with potassium hydroxide solution to hydrolyze the permethric anhydride. After phase separation, toluene is distilled off and the product can be drawn off.

DE 37 05 224 further discloses that the active compound 2,3,5,6-tetrafluorobenzyl-(+)-1R-trans-2,2,-dimethyl-3-(2,2-dichlorovinyl)-cyclopropane-carboxylate (transfluthrin) is obtained by reaction of the salts of (+)-trans-permethric acid with 2,3,5,6-tetrafluorobenzyl chloride according to the following scheme:



For example, the sodium salt of permethric acid is used, and this is reacted with 2,3,5,6-tetrafluorobenzyl chloride, obtainable from the corresponding benzyl alcohol with, for example, $SOCl_2$.

Finally, EP 378 026 generally discloses a process by which compounds of the formula (II)

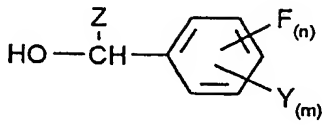


(II)

in which

Hal_1 and Hal_2 can be identical or different and represent fluorine, chlorine, bromine or iodine,

are esterified with benzyl alcohols of the formula



(III)

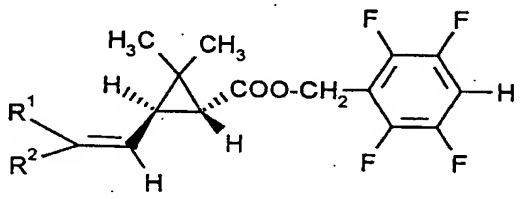
in which

n represents 1 to 5 and

Y can represent, inter alia, hydrogen.

Disadvantages of all of the processes are the complex preparation of the components to be used, which usually have to be prepared in preliminary stages, and the accordingly low total yield of synthetic pyrethroid. A further disadvantage of the process described in the prior art is the occurrence of toxic byproducts, in particular the anhydride of the carboxylic acid used in the particular case.

It has now been found that synthetic pyrethroids of the general formula (I)



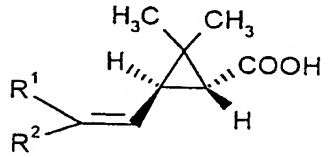
(I)

in which

R^1 represents methyl, difluoromethyl, trifluoromethyl or chlorine and

R^2 represents methyl, difluoromethyl, trifluoromethyl or chlorine,

can be prepared by azeotropic esterification of corresponding carboxylic acids of the general formula (II)



(II)

in which

R^1 and R^2 have the meanings given above, with 2,3,5,6-tetrafluorobenzyl alcohol.

The advantages of this process are based in the simple procedure. The carboxylic acids of the formula (II) need not be converted to the acid chloride, or 2,3,5,6-tetrafluorobenzyl alcohol need not be converted to the corresponding chloride. In addition, during the reaction, anhydrides of the corresponding carboxylic acid are not formed, which generally have unfavorable properties and therefore need to be disposed of with high expenditure.

The process of the invention is suitable in particular for the synthesis of transfluthrin (= 2,3,5,6-tetrafluorobenzyl-(+)-IR-trans-2,2dimethyl-3-(2,2-dichlorovinyl)-cyclopropane-carboxylate).

In the process, the toluene solution of (+)-trans-permethric acid is introduced, 5 to 7 mol% of sulfuric acid is added and the mixture is heated to reflux. With azeotropic removal of water, 80 mol% of tetrafluorobenzyl alcohol are added and the reaction mixture is kept at reflux for a further 4 h.

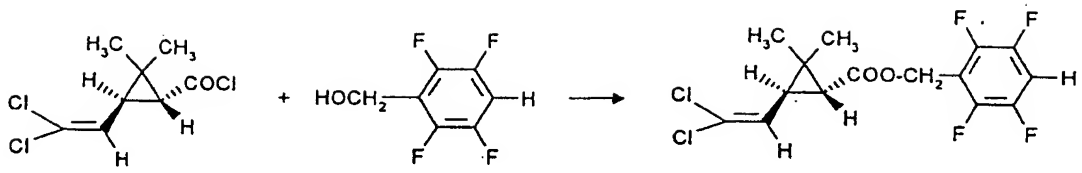
The reaction solution is cooled, the excess acid is extracted as sodium salt with sodium hydroxide solution and reused after the saponification.

Finally, the toluene is distilled off and the active compound remaining in the bottom phase is drawn off.

By means of the present azeotropic esterification process of the invention, on the one hand the yield is increased, and furthermore, shorter cycle times are achieved and thus, overall, higher monthly yields.

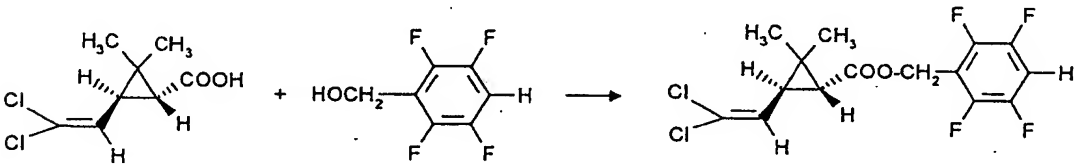
A comparison of the processes makes this clear:

Previous process (A) according to DE 37 05 224



Yield 83%, cycle time 38 hours with batchwise procedure, capacity 18.5 tonnes/month.

Process of the invention (azeotropic distillation); example transfluthrin



Yield 93%, cycle time 18 hours with batchwise procedure, capacity 22 tonnes/month.

The process of the invention is carried out in the presence of a solvent suitable for azeotropic esterification processes. Examples of these solvents which may be mentioned are toluene and benzene.

The reaction temperatures depend in this process on the boiling point of the solvent to be used.

The process of the invention is preferably carried out at atmospheric pressure.

The process of the invention is preferably carried out with a catalyst. The catalysts used are preferably p-toluenesulfonic acid, acidic ion exchangers or sulfuric acid, but in particular sulfuric acid.

In the process of the invention, equimolar amounts of carboxylic acid and 2,3,5,6-tetrafluorobenzyl alcohol are preferably used. However, it has been found that a one to 1.5-fold excess of carboxylic acid has an absolutely beneficial effect on the course of the process (molar ratio: 1.5 mol of carboxylic acid: 1 mol of 2,3,5,6-tetrafluorobenzyl alcohol).

Experimental part

376.2 g (1.8 mol) of (+)-trans-permethric acid are introduced in 860 g of toluene and 8 g of sulfuric acid are added. The batch is heated to reflux and in the course of approximately 1 h, 270 g (1.5 mol) of 2,3,5,6-tetrafluorobenzyl alcohol in 116.0 g of toluene are added; water is simultaneously removed azeotropically. The batch is kept at reflux for a further 4 h, the reaction water being removed azeotropically.

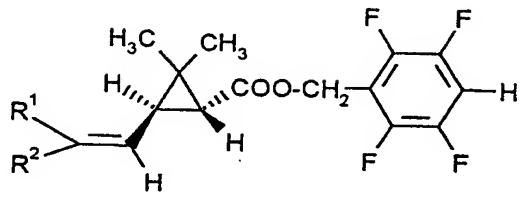
The reaction mixture is cooled to room temperature and extracted with 300 ml of 2 molar sodium hydroxide solution to remove the excess acid.

The organic phase is washed with 500 ml of water and freed from solvent. (The residue is mixed with 250 ml of water and steam-volatile minor components are removed by distilling off water).

Yield: 539.6 g ≡ 97.0% transfluthrin

Patent Claims

1. Process for the preparation of synthetic pyrethroids of the general formula (I)



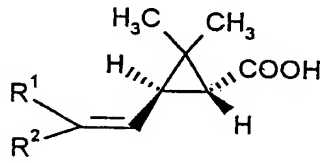
(I)

in which

R^1 represents methyl, difluoromethyl, trifluoromethyl or chlorine and

R^2 represents methyl, difluoromethyl, trifluoromethyl or chlorine,

characterized in that compounds of the formula (II)



(II)

in which

R^1 and R^2 have the meanings given above,

are azeotropically esterified with 2,3,5,6-tetrafluorobenzyl alcohol.

2. Process for the preparation of 2,3,5,6-tetrafluorobenzyl-(+)-1R-trans-2,2-dimethyl-3-(2,2-dichlorovinyl)cyclopropane-carboxylate by azeotropic esterification of (+)-trans-permethric acid with 2,3,5,6-tetrafluorobenzyl alcohol.

3. Process for the preparation of synthetic pyrethroids according to claim 1, characterized in that solvents suitable for azeotropic esterifications are used.

4. Process for the preparation of synthetic pyrethroids according to claim 1, characterized in that the solvent used is toluene.

5. Process for the preparation of synthetic pyrethroids according to claim 1, characterized in that it is carried out under atmospheric pressure.

6. Process for the preparation of synthetic pyrethroids according to claim 1, characterized in that 1 to 1.5 mol of carboxylic acid are azeotropically esterified with 1 mol of 2,3,5,6-tetrafluorobenzyl alcohol.

7. Process for the preparation of synthetic pyrethroids according to claims 1 to 6, characterized in that the process product is free of anhydrides of the carboxylic acids respectively used.

8. Process for the preparation of 2,3,5,6-tetrafluorobenzyl-(+)-1R-trans-2,2-dimethyl-3-(2,2-dichlorovinyl)-cyclopropane-carboxylate, characterized in that a mixture of (+)-trans-permethric acid, toluene and sulfuric acid is heated to reflux, a mixture of 2,3,5,6-tetrafluorobenzyl alcohol in toluene is added, the whole batch is azeotropically esterified finally the reaction mixture is cooled to room temperature and excess acid and solvent are removed.

9. Process for the preparation of synthetic pyrethroids of the general formula (I) substantially as herein described and as exemplified with reference to the Experimental Part.

DATED THIS 13TH DAY OF DECEMBER 1996

JOHN & KERNICK
FOR THE APPLICANT